AMENDMENTS TO THE CLAIMS

1.-6. (Canceled)

7. (Withdrawn) A method of treating, stabilizing or preventing a lower than desired total body weight or a lower than desired percentage of body fat in a mammal comprising:

selecting a mammal in need of treatment for having a lower than desired total body weight or a lower than desired percentage of body fat; and

administering to the mammal a compound that decreases Shp2 activity.

8. (Withdrawn) The method of Claim 7, wherein said compound decreases Shp2 activity in neurons of said mammal.

9. (Withdrawn) The method of Claim 8, wherein said compound decreases Shp2 activity in neurons of forebrain of said mammal.

10. (Withdrawn) The method of Claim 9, wherein said compound decreases Shp2 activity in neurons of hypothalamus of said mammal.

11. (Withdrawn) The method of Claim 7, wherein said compound decreases a level of Shp2 mRNA or protein, an activity of Shp2, a half-life of Shp2 mRNA or protein, or a binding of Shp2 to a leptin receptor.

12. (Withdrawn) The method of Claim 11, wherein said compound is a Shp2 antagonist.

13. (Canceled)

14. (Withdrawn) A screening method for determining a compound useful for treating, stabilizing, or preventing a lower than desired total body weight or a lower than desired percentage of body fat in a mammal, said method comprising

contacting a cell with said compound; and

measuring Shp2 activity in said cell in the presence and absence of the compound, wherein the compound is determined to treat, stabilize, or prevent a lower than desired total body weight or a lower than desired percentage of body fat if the compound decreases the level of Shp2 activity.

15.-25. (Canceled)

26. (Previously presented) A genetically modified mouse comprising a disrupted Shp2 gene, wherein said genetically modified mouse is homozygous for said disrupted Shp2

gene, and wherein said genetically modified mouse exhibits an increased body weight in comparison to a mouse that does not have a disrupted Shp2 gene.

27. (Previously presented) The genetically modified mouse of Claim 26, wherein said Shp2 gene is disrupted in the forebrain of said mouse.

28. (Currently amended) The genetically modified mouse of Claim 26, wherein said mouse has ~~an~~ early-onset obesity.

29. (Previously presented) The genetically modified mouse of Claim 26, wherein said mouse has a resistance to leptin.

30. (Currently amended) The genetically modified mouse of Claim 26, wherein the Shp2 protein level is decreased by 50-70% in the forebrain of said mouse.

31. (Currently amended) The genetically modified mouse of Claim 26, wherein triglyceride levels are increased in the serum of said mouse.

32. (Previously presented) The genetically modified mouse of Claim 26, wherein said Shp2 gene is absent in the forebrain of said mouse.

33. (Currently amended) A method of screening compounds for preventing or ameliorating obesity, comprising:

(a) providing a genetically modified mouse comprising a disrupted Shp2 gene, wherein said genetically modified mouse is homozygous for said disrupted Shp2 gene, and wherein said genetically modified mouse exhibits an accelerated increase of body weight compared to a mouse that does not have a disrupted Shp2 gene;

(b) administering a test compound to said genetically modified mouse;

(c) determining the effect of said test compound on the body weight of said genetically modified mouse; and

(d) correlating a decrease in the body weight of said genetically modified mouse with an anti-obesity effect of said test compound.

34. (New) The method of Claim 33, wherein said Shp2 gene is disrupted in the forebrain of said genetically modified mouse.

35. (New) The method of Claim 33, wherein said Shp2 gene is absent in the forebrain of said genetically modified mouse.

36. (New) The method of Claim 33, wherein said test compound decreases Shp2 activity in neurons of said genetically modified mouse.

37. (New) The method of Claim 36, wherein said test compound decreases Shp2 activity in neurons in the forebrain of said genetically modified mouse.

38. (New) The method of Claim 37, wherein said test compound decreases Shp2 activity in neurons in the hypothalamus of said genetically modified mouse.

39. (New) The method of Claim 33, wherein said test compound is a Shp2 agonist.

40. (New) The method of Claim 33, wherein said test compound is capable of traversing the blood-brain barrier.

41. (New) The method of Claim 33, wherein said test compound is selected from the group consisting of a peptide, an antibody or fragment thereof, and a small molecule.

42. (New) The method of Claim 33, further comprising determining whether said test compound increases the level of a Shp2 mRNA or protein, a Shp2 activity, the half-life of a Shp2 mRNA or protein, or the binding of Shp2 to a leptin receptor.

43. (New) The method of Claim 33, further comprising:

determining the effect of said test compound on the percentage of body fat of said genetically modified mouse; and

correlating a decrease in the percentage of body fat of said genetically modified mouse with an anti-obesity effect of said test compound.